

INOVATE-HF WEBSITE TEMPLATE

STUDY TITLE:

INOVATE-HF (INcrease Of VAgal TonE in Heart Failure)

PRINCIPAL INVESTIGATOR:

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PURPOSE:

INOVATE-HF is designed to investigate the safety and efficacy of the CardioFit™ implantable electrical stimulation device for the treatment of patients with congestive heart failure (HF) and left ventricular dysfunction. INOVATE-HF will evaluate the system's potential to reduce hospitalization and death among patients with HF.

PROTOCOL:

INOVATE-HF is a multi-center, prospective, randomized, controlled clinical study. Patients are randomized on a three-to-two basis with the CardioFit or ongoing prescription drug therapy. The primary efficacy endpoint is time to first occurrence of unplanned HF hospitalization or all-cause death. The primary safety endpoints are system-related complications within 90 days of implantation and non-inferiority to prescription drug therapy beyond 90 days. Secondary endpoints include the rate of unplanned HF hospitalization as well as the change from baseline to 12 months in HF symptoms as well as functional and structural cardiovascular status.

ELIGIBILITY

Inclusion Criteria:

- Age between 18 and 80 years
- New York Heart Association functional class III heart failure diagnosis
- Left ventricular ejection fraction (LVEF) less than or equal to 40% and left ventricular end-diastolic diameter index (LVDDi) 3-4 cm/m
- QRS width \leq 20-msec
- Sinus rhythm, average daytime heart rate between 65 and 110 beats/min via 24-hour Holter within one month
- Stable, optimally uptitrated medical therapy recommended according to current guidelines for a minimum of X months
- 6-minute walk distance at baseline 150 - 425 meters
- NT-ProBNP level 1000 -15000pg/ml, local lab

Exclusion Criteria:

- Presence of life-threatening condition or disease other than HF that is likely to lead to death within 180 days, including cancer, terminal renal failure or a progressive neurological disorder
- Acute myocardial infarction (MI), variant angina pectoris, unstable angina or acute coronary syndrome in the last 30 days
- Previous history of stroke or transient ischemic attack (TIA)
- Coronary artery bypass surgery (CABG), valve replacement or repair, aortic surgery or percutaneous coronary intervention in the last 90 days, or unplanned within 180 days
- HF due to acute myocarditis, restrictive cardiomyopathy, constrictive pericarditis or hemodynamically significant aortic valve insufficiency, aortic stenosis or mitral valve stenosis

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- Severe renal or hepatic failure (creatinine level >3 mg% [265 micromole/liter] or transaminase level four times ULN, or total bilirubin level >1.8 mmol/dL)
- Type I Diabetes Mellitus; Type II Diabetes Mellitus with clinical evidence of diabetic sensory neuropathy (e.g., paresthesis), suspected diabetic autonomic neuropathy (e.g., orthostatic hypotension, early satiety), duration of disease greater than 10 years or measured HgbA1c within the last 60 days above 7.5%
- Previous neck surgery, including cerebrovascular disease (CVD), malignancy, and previous irradiation therapy of the neck (history of left neck surgery for other indications is allowed)
- Current hypotension (systolic blood pressure below 80 mmHg)
- Active peptic ulcer disease or history of upper gastrointestinal bleeding, or ulcer within the last 6 months
- Asthma, history of severe COPD (e.g., FEV₁ <1.5 liter), severe restrictive lung disease or oxygen dependence
- Presence of sustained ventricular tachyarrhythmia with hemodynamic compromise, in the absence of implantable cardiac defibrillator (ICD); recent discharge of an ICD (appropriate or inappropriate) during the last 30 days; ICD on a recall watch list; or planned elective ICD generator change in last 180 days; use of unipolar sensing; or a minimal post-ventricular blanking period shorter than 135-msec in all sensed leads
- Congenital or acquired long QT syndrome
- Documented recorded or suspected vaso-vagal syncope or vaso depressor syncope
- Treatment by investigational drug or device within last 90 days
- Ongoing therapy with Plavix®, the anti-coagulant warfarin or any form of heparin or anti-thrombin agent, unless at the discretion of the principal investigator the drug can be safely discontinued for a minimum of one week prior to and after the CardioFit implant procedure
- Use of class III anti-arrhythmic drugs including amiodarone within three months, calcium channel antagonists that affect SA node (diltiazem or verapril), or inotropic therapy (doputamine, dopamine or milrinone). The subject must not have received inotropic therapy in the last 60 days or be considered as a candidate for inotropic therapy within the next 28 days
- Use of digoxin at doses greater than 1.225 mg per day in the last 60 days or anticipated initiation of digoxin at any time point during the study
- Inability to understand the informed consent and/or prior diagnosis of major affective disorder (e.g., major depression or bipolar disorder or schizophrenia that requires ongoing treatment and is not adequately controlled by medication)
- Subjects transplanted with heart or other tissues or organs, or on a heart transplant waiting list or expected to be on a heart transplant waiting list within the next 180 days
- Immunosuppressed subjects; subjects under systemic steroid treatment
- Anemia with Hgb ≥ 9.5 g/L. Treatment with erythropoietin or other similar agents is allowed if used to keep Hgb > 9.5 g/L
- Subjects who are at risk for carotid artery disease, including subjects with more than 50% carotid artery stenosis assessed on carotid ultrasound, unstable carotid plaques assessed on carotid ultrasound with Doppler, and audible carotid bruit
- Untreated obstructive sleep apnea (OSA) with apnea-hypopnea index of 15 or more, or OSA that has been treated for less than 3 months